



**PATENT APPLICATION**

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re application of

Docket No: Q71975

Levon ARAKELYAN, et al.

Appln. No.: 10/662,345

Group Art Unit: 1631

Confirmation No.: 2068

Examiner: Not Yet Assigned

Filed: September 16, 2003

For: AN INTERACTIVE TECHNIQUE FOR OPTIMIZING DRUG DEVELOPMENT FROM  
THE PRE-CLINICAL PHASES THROUGH PHASE-IV

**INFORMATION DISCLOSURE STATEMENT**  
**UNDER 37 C.F.R. §§ 1.97 and 1.98**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

In accordance with the duty of disclosure under 37 C.F.R. § 1.56, Applicant hereby notifies the U.S. Patent and Trademark Office of the documents which are listed on the attached PTO/SB/08 A & B (modified) form and/or listed herein and which the Examiner may deem material to patentability of the claims of the above-identified application.

One copy of each of the listed documents, other than any U.S. patents and patent publications, is submitted herewith.

The present Information Disclosure Statement is being filed: (1) No later than three months from the application's filing date; (2) Before the mailing date of the first Office Action on the merits (whichever is later); or (3) Before the mailing date of the first Office Action after filing a request for continued examination (RCE) under §1.114, and therefore, no Statement under 37 C.F.R. § 1.97(e) or fee under 37 C.F.R. § 1.17(p) is required.

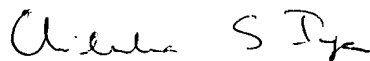
INFORMATION DISCLOSURE STATEMENT

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The submission of the listed documents is not intended as an admission that any such document constitutes prior art against the claims of the present application. Applicant does not waive any right to take any action that would be appropriate to antedate or otherwise remove any listed document as a competent reference against the claims of the present application.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account. A duplicate copy of this paper is attached.

Respectfully submitted,



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Registration No. 43,355

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WASHINGTON OFFICE

**23373**

CUSTOMER NUMBER

Date: January 6, 2004

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Substitute for form 1449/PTO		Complete if Known	
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (Use as many sheets as necessary)		Application Number	
		Filing Date	Sept. 16, 2003
		First Named Inventor	Levon ARAKELYAN
		Art Unit	
		Examiner Name	
Sheet 1 of 5	Attorney Docket Number	Q71975	

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
	1.	FDA, CENTER FOR DRUG EVALUATION AND RESEARCH (CDER), Drug Development Process for Investigational New Drugs, <a href="http://www.fda.gov/cder/handbook/develop.htm">http://www.fda.gov/cder/handbook/develop.htm</a> , pp.3-28	
	2.	DEPARTMENT OF HEALTH AND HUMAN SERVICES, FDA, International Conference on Harmonization: Guidance on General Considerations for Clinical Trials, Federal Register Wednesday, December 17, 1997, pp. 66113-66119, Vol. 62, No. 242	
	3.	E.A. EISENHAUER et al, Phase-I clinical trial design in cancer drug development, J Clin Oncol, Feb., 2000, pp. 684-692, vol. 18(3)	
	4.	R. SIMON et al, Accelerated titration designs for Phase-I clinical trials in oncology, J Natl Cancer Inst, Aug. 6, 1997, pp. 1138-1147, vol. 89(15)	
	5.	J.M. COLLINS et al, Potential roles for pre-clinical pharmacology in Phase-I clinical trials, Cancer Treat Rep, Jan., 1986, pp. 73-80, vol.70(1)	
	6.	Z. AGUR et al, Effect of the dosing interval on survival and myelotoxicity in mice treated by Cytosine arabinoside, Eur. J. Cancer, 1992, pp. 1085-1090, vol. 28A(6/7)	
	7.	L. COJOCARU et al, Theoretical analysis of interval drug dosing for cell-cycle-phase-specific drugs, Math. Biosci., 1992, pp. 85-97, vol. 109	
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	11	Z. AGUR, Use of mathematical models for analyzing host-specific parasitaemia profiles in African trypanosomes, Parasitology Today, 1992, pp. 128-129, vol. 8	
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	19	Z. AGUR et al, Use of knowledge on {fn} series for predicting optimal chemotherapy treatment, Random & Computational Dynamics, 1994, pp. 279-286, vol. 2(3&4)	
	20	Z. AGUR et al, AZT effect on the Bone Marrow-a new perspective on the Concorde Trials, Jour. Biol. Sys, 1995, pp. 241-251, vol. 3(1)	

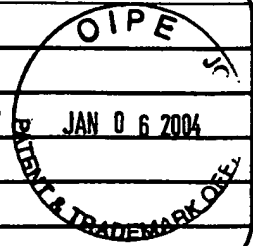
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	21	R. MEHR et al, Temporal stochasticity leads to nondeterministic chaos in a model for blood cell production. in: "Fluctuations and Order: The New Synthesis", 1996, pp. 419-427, Springer, New-York	
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	24	E. SHOCHAT et al, Using Computer Simulations for Evaluating The Efficacy of Breast Cancer Chemotherapy Protocols, Math. Models & Methods in Applied Sciences, 1999, pp. 599-615, vol. 9(4)	
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	26	L. ARAKELYAN et al, A computer algorithm describing angiogenesis and vessel maturation and its use for studying the effects of anti-angiogenic and anti-maturation therapy on vascular tumor growth, Angiogenesis, 2002, pp. 203-214, vol. 5	
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	29	R. SIMON, Therapeutic equivalence trials, Handbook of Statistics in Clinical Oncology, 2001, pp. 173-187, Marcel Dekker, New York	

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	30	A. ILIADIS et al, Optimizing Drug Regimens in Cancer Chemotherapy by an Efficacy-Toxicity Mathematical Model, Computers and Biomedical Research, 2000, pp. 211-226, vol. 33	
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	36	P. BAUER et al, Combining different phases in the development of medical treatments within a single trial, Stat Med, July, 1999; pp. 1833-1848, vol. 18(14)	
	37	E. ARDIZZONE et al, Artificial intelligence techniques for cancer treatment planning, Med Inform (Lond), Jul-Sept., 1988, pp. 199-210, vol. 13(3)	

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	38	D. BERRY, Adaptive Trials and Bayesian Statistics in Drug Development, Biopharmaceutical Report, 2001, pp. 1-11 vol. 9(2)	
	39	D. BERRY, General Keynote: Clinical Trial Design, Gynecological Oncology, 2003, pp. S114-S116, vol. 88	
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